PERSPECTIVE

Can Catheter Ablation Cure Atrial Fibrillation?

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Atrial fibrillation (AF) is the most common sustained arrhythmia in clinical practice. Approximately 6% of those over 60 are affected. Because of the risk of stroke and symptoms related to loss of atrial systole and rapid and/or irregular ventricular response, initial therapy is directed toward reversion to and maintenance of sinus rhythm. However, the pharmacologic approach is being reconsidered because of associated proarrhythmia, long term inefficacy and a possible increase in mortality. Catheter ablation of the atrioventricular (AV) node with pacemaker implantation, or modification of the AV node without pacer implantation, can be useful to facilitate ventricular rate control, but thromboembolic risk is unchanged and atrial systole is not restored. Given the limitations of medical therapy, repeated cardioversions (either externally or via an implanted device) and atrioventricular conduction ablation, an approach that cures atrial fibrillation would be highly desirable.

Moe's concept that during AF there are multiple wandering reentrant waves, combined with the principle of wavelength which implies an adequate spatial extent of contiguous electrically active tissue for wavelets to perpetuate, led to the hypothesis that atrial compartmentalization might prevent AF. Surgical approaches to cure AF include the "corridor procedure" which restores sinus control over the ventricles but leaves a fibrillating atrium, and the Cox "maze procedure" which not only allows return of sinus node control but also restores effective atrial systole in most cases. Recently, Sueda and coworkers (1) have modified the maze operation for patients with mitral valvular disease and AF in a procedure that offers a high cure rate with incisions confined to the back of the left atrium.

While offering hope to patients with intractable atrial arrhythmias, these procedures involve major surgery with its attendant risks and costs. Nevertheless, the "maze" operation teaches an important principle: if the atrium is segmented so that a critical mass is unavailable for Moe's "multiple wavelets," fibrillation ceases and in most cases atrial systolic function is restored over time.

Sub-Types of Atrial Fibrillation

Though the concept of multiple wandering wavelets is appealing, there are still large gaps in our understanding of the pathophysiology of human AF. In addition, it is likely that what we term "atrial fibrillation" is in fact several different disorders with a common electrocardiographic manifestation. For example, an older hypothesis that AF may result from a single focus firing at a rate so rapid that the remainder of the atrium cannot follow synchronously is now being resurrected as it has become clear from mapping studies that some patients indeed have "focal AF" (2). In turn, this observation has important implications for treatment of such patients with catheter ablation. The relative incidence of the various subtypes of AF in patients with paroxysmal or established AF is unknown but is likely to be an important area for future research.

Catheter Ablation for Cure of Atrial Fibrillation

Encouraged by the success of the surgical approach to atrial segmentation, several investigators have reported preliminary clinical results of catheter ablation for cure of AF. Techniques and patient enrollment criteria, as well as success rates, have varied among these early efforts. Some have attempted to make long linear atrial lesions via a "drag" technique whereby radiofrequency (RF) energy is applied through a standard electrode ablation catheter as it is moved incrementally across the endocardium (3–5). Special long vascular sheaths are sometimes used to stabilize the catheter. A recent advance is the use of multielectrode catheters that can be placed against the atrial wall to allow creation of a long linear atrial lesion without catheter dragging (6, 7). However, the technical difficulty of achieving uniform, stable, tissue contact over a long catheter segment across complex atrial anatomy is not to be minimized.

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Table 1. PRELIMINARY RESULTS OF CURATIVE ABLATION FOR ATRIAL FIBRILLATION

Investigator	AF Type	Procedure Type	Left atrial lesions?	N	Success
Haissaguerre et al. (9)	Frequent PAF	Custom multi-electrode catheter, ablate residual focal atrial tachycardia	Yes, in most recent 10	45	13% RA only/no drugs; 40% RA only/plus drugs; 40% RA + LA/no drugs; 70% RA + LA/plus drugs
Swartz et al. (5)	CAF, structural heart disease	Standard catheter, custom sheaths, "drag" lesions	Yes	36	84% at 18 mos
Man et al. (4)	PAF	Standard catheter, "drag" lesions	No	12	33% acute; 25% plus drugs; 8% at 2 mos
Natale et al. (3)	PAF	Standard catheter, "drag" lesions	No	6	67% at 8 mos
Various (including UCSF, 2 from Bordeaux, Tulsa)	Focal	Standard ablation of rapid focal atrial tachycardia mimicking AF	Yes	60?	>90%?
Gaita et al. (8)	"Vagal" (PAF & CAF)	Multi-electrodes in RA	No	14	21% no drugs 42% with drugs
Maloney et al. (10)	CAF	Drag and focal lesions with standard catheter	Yes in 5	8	50% (83% if biatrial procedure)

AF, atrial fibrillation. CAF, chronic atrial fibrillation. LA, left atrium. PAF, paroxysmal atrial fibrillation. RA, right atrium

One advantage of a catheter-based approach over a surgical one is the opportunity to attempt a sequential pattern of lesions. Thus, mitigating the risks associated with left atrial catheterization, some have restricted lesion creation to the right atrium with the hypothesis that a subset of patients, perhaps those with paroxysmal or "vagal" AF and no structural heart disease who are in the "early" stage of progression to a more chronic AF may benefit from such an exclusively right-sided approach (3, 4, 8).

An interesting group of patients are those with "focal" AF. These patients are typically younger, lack structural heart disease, and may have frequent atrial premature beats and runs of atrial tachycardia with a relatively constant P wave morphology, in addition to AF which may appear to degenerate from a burst of atrial tachycardia. The site of origin of these tachycardias is typically in or near the ostia of the upper pulmonary veins, or at the superior aspect of the crista terminalis. Often, one can record local activation with high-frequency spike-like electrograms at cycle lengths as short as 150 ms, with variable exit block from these isolated foci. Because these tachycardias have a focal mechanism, they can be abolished using standard RF ablation electrode catheters (2). However, the pulmonary veins are actually quite large and complex funnel-shaped structures, with atrial tissue extending well into the veins in a heterogeneous fashion. Interestingly, in a recent study from Haissaguerre and colleagues (9), it was shown that in patients with daily bouts of atrial arrhythmia, premature beats arising from the pulmonary veins served as the trigger in 22 of 25 patients, and ablation was effective in eliminating these triggers.

As indicated in Table 1, results of catheter ablation to cure AF have to date been mixed. Complications including stroke, pericardial effusions, and phrenic nerve damage have occurred, and procedures are often lengthy. It should be emphasized, however, that the devices presently available for constructing long linear atrial lesions are far from optimized, and it is likely that the technical goal of creating long, continuous, transmural lesions has not been met in many of the patients treated so far. Therefore, the hypothesis that, for example, a strictly right-sided approach will be useful in a subset of patients cannot be accepted or rejected until one can make lesions with assurance, and even then experimentation with different lesion patterns will be needed. Interestingly, Swartz et al. (5) has achieved what would appear to be a reasonably high success rate creating linear "drag" lesions via special sheaths and a standard 4 mm tipped ablation catheter predominantly using a left atrial approach. Even in these patients with long standing AF, atrial mechanical systole is restored over a period of 3 to 6 months in most. These results are strongly encouraging and point to the great potential, and need, for better, more efficient and safe lesion-creation technology.

It will be important that the lesions not have gaps and that they be linked to anatomic barriers, or new intra-atrial reentrant tachycardias will emerge in analogy to patients with "incisional reentry" following operated congenital heart disease. In our experience, there may be benefit from the adjunctive use of intracardiac echocardiography (ICE) guidance of linear lesion placement. The advantages of ICE includes the identification of anatomic structures (crista terminalis, pulmonary veins, etc.) to which lesions will be linked, the ability to alter catheter positioning to affirm good electrode/tissue contact which is essential for lesion creation, and the direct visualization of lesions that have been made. As is the case for the lesion-creating catheters themselves, improvements are clearly needed in ICE technology so that the catheters provide steerability and better penetration and resolution.

On The Challenges of an Atrial Fibrillation Cure

The history of interventional electrophysiology is repeating itself; it was the success of surgical division of accessory pathways and the AV conduction system that challenged electrophysiologists to develop catheter-based techniques for supraventricular tachycardias such as those associated with the WPW syndrome, which have now become standard of care. However, there are clear differences between catheter ablation for SVT and for AF, and optimism must be tempered by the hard work ahead.

Considerable understanding of the substrate for WPW, for example, was acquired over a number of years during diagnostic electrophysiologic evaluation prior to the era of catheter ablation. In distinction, we still know comparatively little about the anatomic and functional substrate of AF in man and detailed mapping has been performed in only a relatively small number of patients. Furthermore, because of the complex nature of AF, interpreting activation maps can be problematic. Indeed, it is not yet clear whether mapping will even be required for successful catheter ablation of AF.

From a technical standpoint, it is far easier to design, construct and then position in a patient a catheter intended to produce the small focal lesion that is required to cure PSVT than it is to make a device that can create a set of multiple long, linear atrial lesions with the strict limitations created by a transvascular approach. Furthermore, attempts to leverage existing steerable catheter technology, mandated to some extent by the vicissitudes of corporate financing and regulatory approaches, may be less likely successful than truly novel approaches utilizing a top-down approach with platforms designed specifically for AF ablation.

From the standpoint of clinical and regulatory strategy, more than 10,000 RF catheter ablation procedures were performed for PSVT via "off-label" use of clinically available "diagnostic" catheters and RF current generators *before* investigational device exemptions were requested of the Food and Drug Administration (FDA). In other words, RF catheter ablation for SVT was well accepted therapy with superb safety and efficacy profiles, and therefore success of the regulatory approval process was virtually assured. On the other hand, the development of novel devices for creating long linear lesions, overcoming the investigator "learning curve," defining the optimal lesion set, identifying predictors of patients likely to benefit from curative ablation, etc., will all take place in the setting of carefully designed prospective clinical studies under the auspices of regulatory oversight. While this is certainly in the long-term best interest of our patients, it implies that ablation for AF using new devices will mature over at least several years, and only be available at centers participating in FDA-approved, industry-sponsored investigative studies during that time.

Summary

Early results of transcatheter ablation for atrial fibrillation are cause for encouragement and caution. It is likely that within the next 3 to 5 years we will be able to restore sinus rhythm to many patients with drug- and cardioversion-refractory AF. However, many technical and scientific problems need to be addressed during that time if we are to "cure" patients with an efficient, safe, and cost-effective procedure. At present, for example, the best technology (catheter design, energy source) for making atrial lesions and the optimal lesion pattern needs to be defined. Once these technical and scientific issues are addressed, randomized studies will still be needed to show true improvement in outcome and costs compared to conventional approaches. However, if we are able to truly cure this most common of all arrhythmias, we will surely have acquired the "holy grail" of cardiac electrophysiology.

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